OnwarD
A FORWARD STUDY

ALEXION
AstraZeneca Rare Disease

# A Phase 2, Double-Masked, Placebo-Controlled, Dose Range Finding Study of Danicopan (ALXN2040) in Patients With Geographic Atrophy Secondary to Age-Related Macular Degeneration

Dear Health Care Professional,

Alexion Pharmaceuticals Inc. is currently sponsoring a Phase 2 clinical research study of the investigational treatment danicopan in patients with Geographic Atrophy (GA) secondary to Age-Related Macular Degeneration (AMD).

The primary objective of this study is to evaluate the effect of different dosage regimens of danicopan on the progression of GA secondary to AMD compared to placebo.

Danicopan is an oral small molecule inhibitor of Factor D, which is essential to activation of the alternative complement pathway. Dysregulation of the alternative pathway has been implicated in the pathogenesis of AMD.

Danicopan has been shown to be an efficacious inhibitor of Factor D in studies on paroxysmal nocturnal hemoglobinuria. This efficacy, alongside the specific affinity for melanin-containing tissues and the ability to cross the blood-retina barrier, makes danicopan a logical candidate for the treatment of GA.

Participants in this study will receive investigational treatment for up to 2 years and 3 months. Please refer to the opposite side of this letter for more information on the study.

## Do you have eligible patients?

Please consider referring them to the OnwarD Study.

On the web: **theonwardstudy.com**

By phone: _____

Thank you for your consideration.

Sincerely,

_____

## Patient Eligibility Criteria

Select criteria are listed below.

### Inclusion Criteria

- Age ≥ 60 years
- Presentation of GA secondary to AMD in at least one eye
- Study eye must have visual acuity in the specified range (84 to 24 letters; 20/20 to 20/320) using Early Treatment Diabetic Retinopathy Study (ETDRS) charts at a starting distance of 4 meters
- Total GA lesion area of 0.5 to 17.76 $mm^2$ (~0.2 to 7 disc area [DA]) per eye measured by fundus autofluorescence (FAF). If GA is multifocal, at least one focal lesion must be ≥ 0.5 $mm^2$ (~0.2 DA).
- Entire GA lesion must be >1 µm outside of foveal center

### Exclusion Criteria

- GA in the study eye due to cause other than AMD per Investigator's judgment
- GA and concomitant neovascular AMD in the study eye
- Previous intravitreal anti-vascular endothelial growth factor (VEGF) injections in study eye for intraocular vascular disease

## Study Design

The study lasts up to **2 years and 3 months.** During that time, there will be about 15 study clinic visits and 4 home visits (with a visiting health service).

**Screening**
6 weeks

**Masked Treatment***
104 weeks

**Dose Decrease and Follow-up**
6 days + 30 days

*Placebo patients will be re-randomized to one of the 3 active treatment groups at Week 52, or switched to the optimal dose if already identified. If an optimal dose is identified, all patients who have at least 52 weeks of treatment on their original assigned dose will be switched to the selected optimal dose for the remainder of the study. Masked treatment will be maintained throughout the study.

## Treatment Groups

332 patients
aged ≥ 60 years

Randomized
1:1:1:1

**Year 1 treatment:**
100 mg bid
200 mg bid
400 mg qd
Placebo

**Year 2 treatment:**
100 mg bid
200 mg bid
400 mg qd

## Study Endpoints

**Primary endpoint:** Change from Baseline to Week 52 in the square root (sqrt) of total GA lesion area (mm) in the study eye as measured by fundus autofluorescence (FAF).

**Additional endpoints:** Other measures of efficacy, as well as safety and pharmacokinetics.